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Anxiety and its relationship to quality of life independent of depression in patients with obstructive sleep apnea

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ABSTRACT

Objectives: The relationship between anxiety and obstructive sleep apnea (OSA) has not been well studied. We evaluated the factors associated with anxiety and whether anxiety is related to quality of life (QoL) independently of depression in OSA patients.
Methods: Data were collected from adults with newly diagnosed, untreated OSA. The State-Trait Anxiety Inventory–State Scale (STAI-S), the Beck Depression Inventory (BDI), the Epworth Sleepiness Scale (ESS), and the Short Form 36 Health survey (SF-36) were used. Anxiety and depression were defined as high levels of anxiety symptoms (STAI-S score ≥ 40) and depressive symptoms (BDI ≥ 10), respectively. Associations between anxiety and OSA were analyzed using multiple linear regression analysis.
Results: Of 655 OSA subjects included, the prevalence of anxiety and depression was 48.4% and 46.4%, respectively. The scores of STAI-S had strong correlations with BDI ($r = 0.676$, $p < 0.001$). Female sex ($p < 0.05$), excessive daytime sleepiness (ESS ≥ 10) ($p < 0.05$), and a lower educational level ($p < 0.05$) were identified as independent factors for predicting the presence of anxiety in OSA patients. The severity of OSA measured by the apnea–hypopnea index or respiratory distress index was not related to comorbid anxiety. In linear regression analysis, both anxiety (ß = −10.196, $p < 0.001$) and depression (ß = −16.317, $p < 0.001$) were independently associated with lower SF-36 scores in OSA patients.
Conclusions: The presence of anxiety can be predicted by female sex, daytime sleepiness, and a lower educational level. Both anxiety and depression were independently associated with a lower QoL in OSA patients.

Introduction

Obstructive sleep apnea (OSA) is the most common type of sleep apnea [1]. The characteristic feature of OSA is a transient and repetitive obstruction of the upper airway during sleep. These episodes of airway obstruction cause intermittent periods of oxygen desaturation and arousal from sleep, resulting in fragmented sleep. The prevalence of OSA was estimated from large population studies, such as the Sleep Heart Health study, to be up to 18% [2]. Untreated OSA is often associated with cardiovascular disease [3,4]. Symptoms reported by OSA patients include fatigue, daytime sleepiness, poor sleep quality, impaired concentration, memory loss, headache, and mood and affect disturbance [5]. OSA has a significant impact on individuals' daytime functioning, increasing traffic accidents and decreasing work productivity [6].

The physical effects of OSA and its treatment have been extensively investigated, but the psychological aspects of OSA, especially anxiety, have not drawn as much attention [7]. In fact, the relationship between anxiety and OSA is not addressed in the clinical guidelines for the management of OSA [8]. The prevalence of anxiety ranges from 11% to 70% [7] in OSA patients and individuals with a diagnosis of sleep apnea have increased odds of receiving anxiety disorder diagnosis [9], whereas the relationship between anxiety and OSA is unclear [7]. For example, the severity of OSA was not found in previous investigations to be related to accompanying anxiety [5,7,10]. In addition, the effectiveness of continuous positive airway pressure (CPAP) treatment on anxiety is not consistent in the literature [7]. For example, Kingshott et al. [11] reported that anxiety significantly declined after 6 months of CPAP treatment. In contrast, Munoz et al. [12] failed to find a significant decline in anxiety after 3 and 12 months of CPAP treatment.

Although the role of OSA as a cause of anxiety is still unknown, it is clear that the presence of comorbid anxiety significantly impacts the health-related quality of life (QoL) of OSA patients [13]. In other diseases, depression is considered to be an extremely important determinant of QoL. For example, depression has a greater negative impact on QoL in patients with epilepsy than other clinical indicators such as seizure frequency [14]. In light of the strong association of depression and anxiety with OSA [10,13], it is possible that they strongly affect the QoL of OSA patients. However, the relationship between these mood disturbances and QoL in patients with OSA has not been well

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studied [13]. Therefore, in our current study, we investigated the relationship between OSA and comorbid anxiety in newly diagnosed, untreated OSA patients. The aims of our present analyses were threefold: (1) to determine the prevalence of anxiety in OSA patients; (2) to identify the factors associated with anxiety in OSA patients; and (3) to determine whether anxiety is related to QoL independently of the status of depression in OSA patients.

Methods

Subjects

This study design was cross sectional. Participants were adult patients who visited sleep laboratories for evaluation of suspected OSA between 2009 and 2011. Their chief complaints were OSA-related symptoms such as snoring, stopping breathing during sleep, choking, gasping during sleep, or excessive daytime sleepiness (EDS). They were recruited from a single tertiary hospital in Korea. Basic demographic information, medical comorbidity, and medication information were obtained from the self-reported checklist for medical history and the patient's electronic medical record. The inclusion criteria were as follows: aged above 18 years, undertook an overnight polysomnography (PSG) for suspected OSA, and diagnosed with OSA [apnea–hypopnea index (AHI) ≥ 5/h]. Patients were excluded if they had a periodic limb movement arousal index ≥5/h, if they had psychiatric or medical disorders based on the self-reported checklist for medical history and the patient's electronic medical record, if they were previously diagnosed with and treated for OSA, or if they filled out questionnaires incompletely. We did not exclude patients whose Beck Depression Inventory (BDI) or State-Trait Anxiety Inventory (STAI)–State Scale (STAI-S) scores were over the threshold of depression or anxiety disorder if they had not been previously diagnosed with a psychiatric disorder or were taking medication for the treatment of their condition. The study was reviewed and approved by the Institutional Review Board of the Asan Medical Center.

Polysomnography

OSA was diagnosed using the standard PSG. Apnea, hypopnea, and respiratory effort-related arousal were scored according to the American Academy of Sleep Medicine guidelines [15]. An apnea was defined as a drop in the peak thermal sensor excursion of ≥90% of the baseline value for at least 10 s. A hypopnea was defined as a nasal pressure signal excursion drop of ≥30% of the baseline value for at least 10 s, accompanied by a ≥4% reduction in O_2 saturation from the pre-event baseline. AHI was defined as the average number of episodes of apnea and hypopnea per hour. The respiratory distress index (RDI) was defined as the average number of episodes of apnea, hypopnea, and respiratory effort-related arousal per hour.

Instruments

On the night of the PSG, patients completed a battery of questionnaires that was routinely administered to all patients undergoing PSG at our sleep laboratory.

The presence and severity of current symptoms of anxiety (state-anxiety level) was assessed using State Scale of the STAI [16]. The Trait Scale of the STAI evaluating a generalized propensity to be anxious (trait-anxiety level) was not used in this study. For anxiety assessment, individuals rate themselves on each statement using a Likert scale, with responses from 1 (not at all) to 4 (very much so) based on how they feel at that moment. The range of scores is between 20 and 80; the higher the score, the higher the level of anxiety. Because a cutoff point of ≥40 for the STAI-S has been suggested to detect clinically significant symptoms [17], anxiety was defined as high level of anxiety symptoms (STAI-S score ≥ 40). We used the Korean version of the STAI-S [18].

Daytime sleepiness was evaluated using the Epworth Sleepiness Scale (ESS). The ESS is a self-report, 8-item questionnaire for measuring EDS in everyday situations. The Korean version of the ESS was recently validated [19]. Higher scores indicate greater sleepiness during daily activities.

The BDI is a 21-item, self-report measure assessing the patient's current level of depression. Each item is rated on four-point scale (0–3), with a total possible score range of 0 to 63. Higher scores represent higher levels of depression. In this study, depression was defined as high level of depressive symptoms (BDI ≥ 10). The Korean version of the BDI has also been validated [20].

QoL was assessed using the Medical Outcomes Study Short Form Health Survey (SF-36) [21]. The SF-36 is a multipurpose, self-administered, and non-disease-specific health survey consisting of 36 questions divided into eight individual domains. All domain scores are transformed, resulting in scale scores from 0 (lowest level of functioning) to 100 (highest level of functioning). A higher score indicates a better health-related QoL. The Korean version of the SF-36 was recently validated [21].

Statistical analysis

Several continuous variables such as STAI-S, BDI, ESS, and AHI were dichotomized and analyses were conducted in terms of group differences rather than individual differences because the severity of OSA was not found in previous investigations to be related to accompanying anxiety and depression [5,7,10]. The dependent variable was the presence or absence of anxiety in OSA patients. We dichotomized OSA patients into two groups according to the STAI-S: the presence (STAI-S score ≥ 40) and the absence (STAI-S score < 40) of anxiety. The relationship between independent variables and anxiety status was evaluated by univariate and multivariate analyses. The independent variables included in the analysis were age, sex, body mass index (BMI), educational level (university vs. high or middle school), marital status (married vs. single), employment status (employed vs. unemployed), AHI (mild, moderate, and severe), and the presence or absence of EDS (ESS scores ≥10 vs. <10). For univariate analysis, a Student's *t*-test was used for numeric variables, and a chi-square test was used for nominal variables. Multivariate analysis using binary logistic regression was performed to further assess variables with $p < 0.05$ according to the univariate analysis.

To determine whether a relationship between anxiety and QoL measured by the SF-36 is independent of the depressive mood in OSA patients, we used linear regression analysis. The confounding variables included in the analysis were age, sex, BMI, educational level (university vs. high or middle school), EDS (ESS ≥ 10 vs. <10), and the status of depression (BDI scores ≥10 vs. <10). The significance level was set at $p < 0.05$. Data were analyzed using SPSS version 21.0 (SPSS Inc., Chicago, IL).

Results

Patient characteristics

Of 863 consecutive patients who underwent overnight PSG for suspected OSA, 774 were diagnosed with OSA (AHI ≥ 5/h). Of these, 119 patients were excluded, due to medical problems (cardiac disease, $n = 13$; pulmonary disease, $n = 9$; cancer, $n = 6$; thyroid problems, $n = 5$; gastrointestinal disorder, $n = 4$; and other problems, $n = 3$), neurologic disease ($n = 15$), psychiatric disease (major depression, $n = 5$; panic disorder, $n = 2$; bipolar disorder, $n = 1$; and schizophrenia, $n = 1$), sleep disorder ($n = 4$), previous diagnosis with and treatment for OSA ($n = 6$), a periodic limb movement arousal index ≥5/h ($n = 30$), and incomplete data ($n = 15$). The remaining 655 OSA subjects (569 men and 86 women) participated in the study (Table 1). The average age was 49.8 years (SD = 11.7 years). The mean AHI was 28.5/h (SD = 20.1/h). Of these patients, 205 (31.3%) were classified as having mild OSA (5/h ≤ AHI < 15/h), 199 (30.4%) as having moderate OSA (15/h ≤ AHI < 30/h), and 251 (38.3%) as having severe OSA (AHI ≥ 30/h).

The mean STAI-S score was 34.0 (SD = 16.9). The prevalence of clinically significant anxiety (STAI-S ≥ 40) in the whole group was 48.4%. Severe anxiety (STAI-S ≥ 55) was identified in 7.5% of OSA patients. The mean BDI score was 10.1 (SD = 7.2). The prevalence

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Table 1
Patient characteristics ($n = 655$)

Male, *n* (%)	569 (86.9)
Age, year (SD)	49.8 (11.7)
Body mass index (SD), kg/m^2	25.9 (3.4)
Married, *n* (%)	542 (82.7)
Employed, *n* (%)	616 (94.0)
University education, *n* (%)	354 (54.0)
Apnea–hypopnea index, mean (SD)	28.5 (20.1)
AHI ≥ 30, *n* (%)	251 (38.3)
30 > AHI ≥ 15, *n* (%)	199 (30.4)
15 > AHI ≥ 5, *n* (%)	205 (31.3)
Respiratory distress index, mean (SD)	35.8 (19.1)
RDI ≥ 30, *n* (%)	366 (55.9)
30 > RDI ≥ 15, *n* (%)	219 (33.4)
15 > RDI ≥ 5, *n* (%)	70 (10.7)
PLM index, /h (SD)	5.7 (14.1)
PLM arousal index, /h (SD)	0.4 (0.9)
Short Form-36 questionnaire, mean (SD)	71.7 (19.0)
Epworth Sleepiness Scale, mean (SD)	9.8 (4.9)
≥10, *n* (%)	312 (47.6)
State-Trait Anxiety Index–State, mean (SD)	34.0 (16.9)
≥40, *n* (%)	317 (48.4)
≥55, *n* (%)	49 (7.5)
Beck Depression Inventory, mean (SD)	10.1 (7.2)
≥10, *n* (%)	304 (46.4)

AHI: apnea–hypopnea index; PLM: periodic leg movement; RDI: respiratory distress index; SD: standard deviation.

of depression (BDI ≥ 10) was 46.4%. Patient characteristics are shown in Table 1. The mean total SF-36 score was 71.7 (SD = 19.0). The mean ESS score was 9.8 (SD = 4.9). The prevalence of EDS (ESS ≥ 10) was 47.6%.

Factors related to anxiety in OSA patients

In univariate analysis, a higher prevalence of anxiety was observed in women ($p < 0.001$) and those with EDS ($p = 0.003$), single status ($p = 0.011$), and a lower educational level (high or middle school) ($p < 0.001$) (Table 2). The prevalence of anxiety was 67.5% in women and 54.5% in OSA patients with EDS compared with 45.5% in men and 42.9% in those without EDS. Age, BMI, employment status, and the category of AHI severity were not related to the presence of anxiety in OSA patients. In binary logistic linear regression, female sex, EDS, and a lower educational level were identified as independent factors for predicting the presence of anxiety in OSA patients (Table 3).

Table 2
Comparison of variables between OSA patients with and without anxiety

	OSA with anxiety ($n = 317$)	OSA without anxiety ($n = 338$)	*p* value
Age, year (SD)	50.3 (11.5)	49.2 (11.9)	0.248
Sex			<0.001
Male, *n* (%)	259 (45.5)	310 (54.5)	
Female, *n* (%)	58 (67.4%)	28 (32.6)	
Body mass index (SD), kg/m^2	25.8 (3.4)	26.0 (3.3)	0.387
Epworth Sleepiness Scale			0.003
≥10, *n* (%)	170 (54.5)	142 (45.5)	
<10, *n* (%)	147 (42.9)	196 (57.1)	
Marriage			0.011
Married, *n* (%)	250 (46.1)	292 (53.9)	
Single, *n* (%)	67 (59.3)	46 (40.7)	
Employment			0.090
Employed, *n* (%)	293 (47.6)	323 (52.4)	
Unemployed, *n* (%)	24 (61.5)	15 (38.5)	
Education			<0.001
University, *n* (%)	138 (39.0)	216 (61.0)	
High or middle school, *n* (%)	179 (59.9)	120 (40.1)	
Apnea–hypopnea index			0.296
15 > AHI ≥ 5, *n* (%)	108 (52.7)	97 (47.3)	
30 > AHI ≥ 15, *n* (%)	95 (47.7)	104 (52.3)	
AHI ≥ 30, *n* (%)	114 (45.4)	137 (54.6)	
Respiratory distress index			0.419
15 > RDI ≥ 5, *n* (%)	37 (52.9)	33 (47.1)	
30 > RDI ≥ 15, *n* (%)	111 (50.7)	108 (49.3)	
RDI ≥ 30, *n* (%)	169 (46.2)	197 (53.8)	
Short Form-36 questionnaire, mean (SD)	61.6 (19.1)	81.2 (13.5)	<0.001

AHI: apnea–hypopnea index; OSA: obstructive sleep apnea; PLM: periodic leg movement; RDI: respiratory distress index; SD: standard deviation.

Table 3
Logistic linear regression analysis of the factors associated with anxiety in patients with obstructive sleep apnea

	Non-standardized coefficient	Standard error	Wald	*p* value
Female (reference: male)	0.645	0.259	6.179	0.013
ESS ≥ 10 (reference: <10)	0.398	0.163	5.961	0.015
Middle or high school (reference: university)	0.734	0.166	19.642	0.000
Single (reference: married)	0.382	0.220	3.022	0.082

Dependent variable = the scores of State-Trait Anxiety Index–State.

Dependence of the relationship between anxiety and QoL on the depressive mood in OSA patients

The scores of STAI-S had strong correlations with BDI ($r = 0.676$, $p < 0.001$) (Table 4). Of a total 655 participants, 35.3% ($n = 231$) had both anxiety and depression, 11.1% ($n = 73$) had only depression without anxiety, 13.1% ($n = 86$) had only anxiety without depression, and 40.5% ($n = 265$) had neither anxiety nor depression. Participants with anxiety were more likely to have depression than those without anxiety (72.9% vs 21.6%, $p < 0.001$). There were no sex differences in association between anxiety and depression (odds ratio 21.5, 95% confidence interval 10.2 ~ 45.4 for men vs. odds ratio 16.0, 95% confidence interval 3.5 ~ 73.8 for women, $p = 0.733$)

In linear regression analysis, the presence of anxiety (ß = −10.196, $p < 0.001$) was identified as one of the independent factors for predicting a lower total SF-36 score (Table 5). Age, sex, BMI, and depressed mood were independently associated with a lower total SF-36 score (Table 5). Based on the standardized coefficient, the strongest predictor of the total SF-36 score was the presence of depression (BDI score ≥ 10) (ß = −16.317, $p < 0.001$). The second most important predictor was the presence of anxiety (STAI-S score ≥ 40).

Discussion

We here investigated the relationship between OSA and anxiety in newly diagnosed, untreated OSA patients. The prevalence of comorbid anxiety was 48.5% in our series. Based on binary logistic linear regression, female sex, EDS, and a lower educational level were independent factors for predicting anxiety in OSA patients. Apnea severity measured by AHI and RDI was not found to be related to anxiety. In addition, a relationship between anxiety and QoL measured by SF-36 was found to be independent of depressive mood in OSA patients.

In the literature, the prevalence of anxiety is between 11% and 17% in unselected OSA patients [5,22–24] but is much higher (50% to 70%) in selected OSA patients, such as those receiving CPAP treatment or surgical therapy [25–27]. In our present study series, which included unselected patients with newly diagnosed, untreated OSA, the rate of anxiety was relatively high (48.5%). This high rate can be attributed to factors such as the patient characteristics and the questionnaires used to assess anxiety. In addition, the high anxiety rate could be partly explained by the source of the participants (a tertiary sleep center) and the large proportion of more severe OSA patients who deserved to receive CPAP treatment. In our current sample, two-third of patients had moderate to severe OSA with AHI ≥ 15.

It is unclear why comorbid anxiety is highly prevalent in OSA. Mood and affect disturbances could arise from neural injuries that occur in this condition [28,29]. Kumar et al. [28] found permanent structural brain abnormalities using magnetic resonance imaging in anxious OSA patients; these changes were particularly pronounced in the cortices, thalamus, hippocampus, and amygdale. Recently, Yadav et al. [29] investigated metabolic changes in OSA patients in the insular cortex using proton magnetic resonance spectroscopy and found positive correlations between right insular choline/creatine (Cho/Cr) ratios and BDI-II and Beck Anxiety Inventory scores, suggesting that the metabolically abnormal sites may contribute to the elevated depression and anxiety.

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Table 4
Relationships between anxiety and depression in patients with obstructive sleep apnea

	Men ($n = 569$)				Women ($n = 86$)			
	STAI-S scores	With anxiety	Without anxiety	p value	STAI-S scores	With anxiety	Without anxiety	p value
BDI								
<10, n (%)		78 (23.9)	248 (76.1)	<0.001		8 (32.0)	17 (68.0)	<0.001
≥10, n (%)		181 (74.5)	62 (25.5)			50 (82.0)	11 (18.0)	
Pearson correlation, r	0.671			<0.001	0.668			<0.001

BDI: Beck Depression Inventory; STAI-S: State-Trait Anxiety Index–State Scale.
% within cases with or without depression.

Persons with sleep apnea more frequently have depression and anxiety than those without this condition [22]. However, relationships between OSA severity and psychological symptoms have not been found in most previous studies [5,7,13,30–32]. The severity of OSA is usually measured by AHI or RDI. In our present study, anxiety was also not found to be associated with OSA severity (measured with AHI or RDI). However, the presence of OSA, diagnosed primarily based on AHI values, was previously associated with abnormally high levels of depressive and anxious symptoms [22]. This result suggested that mechanisms other than the number and frequency of hypoxic events contribute to depression and anxiety in this patient population. For example, anxiety has been reported to be more associated with EDS rather than with hypoxemia [13,32]. EDS could be considered either an outcome or an alternative indicator of OSA severity. We also included daytime sleepiness in our current analyses as one of potential variables contributing to anxiety and found that comorbid anxiety is more frequent in OSA patients with EDS, even after controlling for several confounding factors such as age, sex, and BMI. A similar relationship between depression and daytime sleepiness has been described in an earlier study of OSA patients [3]. In contrast, Borak et al. [27] found that anxiety levels were significantly related to AHI values ($r = 0.68$) in 20 patients with severe OSA. Yadav et al. [29] also found significant positive correlations between left insular myo-inositol/creatine (MI/Cr) ratios and AHI values.

Recently, Asghari et al. [32] reported that the severity of depressive and anxiety symptoms was significantly higher in women than in men and suggested that this difference could be due to the significant age difference between the men and the women in their study. In our present study, however, this gender difference in anxiety was confirmed to be independent of age after controlling for several variables, including age. In the general population, there is a higher incidence of affective disorders in women than in men [33]. In addition, there is evidence of gender differences in the clinical presentation of OSA. Men experience OSA at two to three times the rate of women [2] and have a higher AHI than women [34]. However, women with OSA are more likely to report depression and anxiety [13,35], which may be associated with sex-related variations in neural injury occurring with the disorder. Macey et al. [36] have reported that sex differences in white matter structural integrity were present in OSA patients, with females more affected than males. These white matter structural changes may contribute to, or derive from, neuropsychological and physiological differences in symptoms between men and women.

Although the link between psychological problems and QoL in OSA has not been well investigated to date, a strong association of depression and anxiety with OSA has been described [10,13]. Thus, we assumed that psychological problems may have a strong effect on QoL in patients with OSA. Ye et al. [13] examined anxiety and depression to find determinants of QoL in OSA patients and found that anxiety but not depression was the stronger independent predictor of QoL. In their study, depression lost its statistical significance for QoL in multiple regression analysis. The findings of that study are not consistent with our present findings that both depression and anxiety are important independent factors for predicting lower QoL after controlling for confounding variables such as age, sex, BMI, and EDS. Based on the standardized coefficient, a depressive mood was the most important predictor of QoL identified in our present OSA patients, with anxiety symptoms the next most important predictor. Kwan et al. [37] have determined the relative contributions of subjective anxiety, depression, sleep disturbance, and seizure-related variables to QoL in adults with epilepsy and found that both depression and anxiety are significant predictors of QoL. Further studies are needed to explore these relationships in patients with OSA.

Certain limitations should be noted when interpreting the results of our present study. First, our study population was derived from a single tertiary sleep laboratory. Two-thirds of our sample had moderate to severe OSA with an AHI ≥ 15. Hence, some of our results may not be generalizable to other populations. However, our identification of factors contributing to anxiety or QoL in OSA patients should be generally applicable. Second, this was a cross-sectional study and cannot therefore address issues of causality.

In conclusion, anxiety in OSA patients can be predicted by female sex, daytime sleepiness, and a lower educational level. The severity of OSA measured by AHI or RDI is not related to comorbid anxiety. In addition, both anxiety and depressive symptoms are independently associated with lower QoL in OSA patients.

Table 5
Linear regression analysis of the factors associated with quality of life in patients with obstructive sleep apnea

	Non-standardized coefficient	Standard error	Standardized coefficient	p value
Age	−0.123	0.049	−0.076	0.013
Female (reference: male)	−5.375	1.745	−0.095	0.002
Body mass index, kg/m^2	−0.516	0.168	−0.091	0.002
Middle or high school (reference: university)	−1.539	1.182	−0.040	0.193
ESS ≥ 10 (reference: <10)	−1.754	1.133	−0.046	0.122
STAI-S ≥ 40 (reference: <40)	−10.196	1.309	−0.268	0.000
BDI ≥ 10 (reference: <10)	−16.317	1.324	−0.427	0.000

Dependent variable = the scores of Short Form-36. ESS: Epworth Sleepiness Scale; STAI-S: State-Trait Anxiety Index–State Scale; BDI: Beck Depression Index.

Competing interest statement

The authors have no competing interests to report.

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